

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method of making a tobacco product that has a reduced potential to contribute to a tobacco-related disease comprising:
 - (a) providing a first tobacco product; that comprises a compound that contributes to a tobacco-related disease;
 - (b) obtaining smoke or a smoke condensate from said first tobacco product;
 - (c) contacting a first isolated population of cells with said smoke or smoke condensate from said first tobacco product;
 - (d) identifying a first gene that is expressed measuring the level of expression of NM_003900 Sequestosome 1 in said first population of cells in response to said contact with said smoke or smoke condensate from said first tobacco product; , wherein expression of said first gene contributes to a tobacco-related disease;
 - (e) providing a second tobacco product; that has been modified to reduce expression of a second gene;
 - (f) obtaining smoke or a smoke condensate from said second tobacco product;
 - (g) contacting a second isolated population of cells with said smoke or smoke condensate from said second tobacco product;
 - (h) identifying a reduction in measuring the level of expression of said first gene that contributes to a tobacco-related disease NM_003900 Sequestosome 1 in said second population of cells, which are contacted in response to said contact with said smoke or smoke condensate from said second tobacco product; and
 - (i) making said tobacco product from said second tobacco, wherein said tobacco product comprising said second tobacco has a reduced potential to contribute to a tobacco-related disease as compared to a tobacco product comprising said first tobacco, comparing the level of expression of NM_003900 Sequestosome 1 in said first population of cells measured in step (d) with the level of expression of NM_003900 Sequestosome 1 in said second population of cells measured in step (h); and

(j) selecting the tobacco product that has a reduced expression of NM_003900 Sequestosome 1.

2. **(Currently Amended)** The method of Claim 1, wherein said first tobacco product and said second tobacco product comprise is a burley tobacco.

3. **(Currently Amended)** The method of Claim 1, wherein said first tobacco product and said second tobacco product comprise is a flue tobacco.

4. **(Currently Amended)** The method of Claim 1, wherein said first tobacco is an oriental tobacco second tobacco product comprises a modified tobacco.

5. **(Cancelled).**

6. **(Currently Amended)** The method of Claim 1, wherein said first tobacco product and said second tobacco product are cigarettes, and second populations of cells are the same cell type.

7. **(Currently Amended)** The method of Claim 4 6, wherein said cigarettes comprise a filter, first and second populations of cells are immortal cells.

8. **(Original)** The method of Claim 1, wherein said first and second populations of cells are normal human cells of the lung, mouth, or tongue.

9. **(Original)** The method of Claim 1, wherein said first and second populations of cells are normal human bronchial epithelial (NHBE) cells.

10. **(Currently Amended)** The method of Claim 1, further comprising measuring the level of expression of a second gene in said first and second population of cells after contacting said first and second populations of cells with said whole smoke, wherein said second gene that has been modified in said second tobacco is a gene in a pathway of nicotine synthesis.

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11. (Currently Amended) The method of Claim 10, wherein said second gene is selected from the group consisting of: AK054816 Ferritin heavy polypeptide, NM_005345 Heat Shock 70kD protein 1A, NM_003330 Thioredoxin reductase 1, NM_002133 Heme oxygenase (decycling) 1, and NM_000963 Prostaglandin-endoperoxide synthase 2, putrescine N-methyltransferase, N-methylputrescine oxidase, ornithine decarboxylase, S-adenosylmethionine synthetase, NADH dehydrogenase, phosphoribosylanthranilate isomerase, and quinolinate phosphoribosyl transferase (QPTase).

12-52. (Cancelled).